

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Hewick, Rodney M.

Wang, Jack H.

Wozney, John M.

Celeste, Anthony J.

(ii) TITLE OF INVENTION: Bone and Cartilage Inductive Proteins

(iii) NUMBER OF SEQUENCES: 15

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Legal Affairs, Genetics Institute, Inc.

(B) STREET: 87 CambridgePark Drive

(C) CITY: Cambridge

(D) STATE: MA

(E) COUNTRY: USA

(F) ZIP: 02140

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

(B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: US 07/800,364

(B) FILING DATE: 26-NOV-1991

(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Kapinos, Ellen J.

(B) REGISTRATION NUMBER: 32,245

(C) REFERENCE/DOCKET NUMBER: GI 5182A

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 617-876-1170

(B) TELEFAX: 617-876-5851

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp Trp
1 5 10 15

Val Ile Ala Pro Gln Gly Tyr
20

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus
- (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile
1 5 10 15

Leu Arg

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus
- (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Ala Cys Cys Ala Pro Thr Lys
1 5

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus
- (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Thr Asn Glu Leu Pro Pro Pro Asn Lys Leu Pro Gly Ile Phe Asp Asp
1 5 10 15

Val His Gly Ser His Gly Arg
20

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 80 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
 (A) ORGANISM: *Bos taurus*

(vii) IMMEDIATE SOURCE:
 (B) CLONE: acc30

(viii) POSITION IN GENOME:
 (C) UNITS: bp

(ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 25..57

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GGATCCGCGT GCTGTGCTCC GACC AAG CTG AGC GCC ACC TCC GTG CTC TAC

Lys Leu Ser Ala Thr Ser Val Leu Tyr
 1 5

51

TAC GAC AGCAGCAACA ATGTAATTCT AGA
 Tyr Asp
 10

80

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 11 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp
 1 5 10

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 199 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Bos taurus*

(vii) IMMEDIATE SOURCE:

(A) LIBRARY: Bovine genomic
(B) CLONE: Lambda 9800-10

(viii) POSITION IN GENOME:

(C) UNITS: bp

(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 30..199

(ix) FEATURE:

(A) NAME/KEY: intron
(B) LOCATION: 1..29

(ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 30..179

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TGCCCCCTGC CCCCTCCCCG CCCCCGCCAG GTG CAC CTG CTG AAG CCG CAC GCG 53
Val His Leu Leu Lys Pro His Ala
1 5

GTC CCC AAG GCG TGC TGC GCG CCC ACC AAG CTG AGC GCC ACT TCC GTG 101
Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val
10 15 20

CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC CGC AAC 149
Leu Tyr Tyr Asp Ser Ser Asn Val Ile Leu Arg Lys His Arg Asn
25 30 35 40

ATG GTG GTC CGC GCC TGC GGC TGC CAC TGAGGCCCA ACTCCACCGG 196
Met Val Val Arg Ala Cys Gly Cys His
45 50

CAG 199

(2) INFORMATION FOR SEO ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 49 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Val His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro
 1 5 10 15

Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn
 20 25 30

Val Ile Leu Arg Lys His Arg Asn Met Val Val Arg Ala Cys Gly Cys
 35 40 45

His

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 172 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus

(vii) IMMEDIATE SOURCE:

- (A) LIBRARY: Bovine genomic
- (B) CLONE: Lambda 9800-10

(viii) POSITION IN GENOME:

- (C) UNITS: bp

(ix) FEATURE:

- (A) NAME/KEY: exon
- (B) LOCATION: 51..161

(ix) FEATURE:

- (A) NAME/KEY: intron
- (B) LOCATION: 1..50

(ix) FEATURE:

- (A) NAME/KEY: intron
- (B) LOCATION: 162..172

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 51..161

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GGGGTGGGAG GGCACGTGGA TGGGACTCAC CTTCTCCAC TACCCCCCAG GAC TGG 56
 Asp Trp
 1

GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG GAG TGC 104
 Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys
 5 10 15

TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG 152
 Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu
 20 25 30

CAG TCC CTG GTCAGTACCT C 172
 Gln Ser Leu
 35

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 37 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly
 1 5 10 15

Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala
 20 25 30

Ile Leu Gln Ser Leu
 35

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 119 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Bos taurus

(vii) IMMEDIATE SOURCE:

(A) LIBRARY: Bovine genome
(B) CLONE: Lambda 9800-10

(viii) POSITION IN GENOME:

(C) UNITS: bp

(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 20..99

(ix) FEATURE:

(A) NAME/KEY: intron
(B) LOCATION: 1..19

(ix) FEATURE:

(A) NAME/KEY: intron
(B) LOCATION: 100..119

(ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 22..99

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

CCCTTGCCTG TCCCCGCAGA C GAC GTC CAC GGC TCC CAC GGC CGG CAG GTG 51
 Asp Val His Gly Ser His Gly Arg Gln Val
 1 5 10

TGC CGT CGG CAC GAG CTG TAC GTG AGC TTC CAG GAC CTG GGC TGG CTG 99
 Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu
 15 20 25

GTGAGTTCCG ACTCTCCTTT 119

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Glu Leu
 1 5 10 15

Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu
 20 25

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1003 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (F) TISSUE TYPE: Human Heart

(vii) IMMEDIATE SOURCE:

- (A) LIBRARY: Human heart cDNA library stratagene catalog
#936208
- (B) CLONE: hH38

(viii) POSITION IN GENOME:

- (C) UNITS: bp

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 8..850

(ix) FEATURE:

- (A) NAME/KEY: mat_peptide
- (B) LOCATION: 427..843

(ix) FEATURE:

- (A) NAME/KEY: mRNA
- (B) LOCATION: 1..997

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

GAATTCC GAG CCC CAT TGG AAG GAG TTC CGC TTT GAC CTG ACC CAG ATC
 Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile
 -139 -135 -130

CCG GCT GGG GAG GCG GTC ACA GCT GCG GAG TTC CGG ATT TAC AAG GTG Pro Ala Gly Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Val	97
-125 -120 -115 -110	
CCC AGC ATC CAC CTG CTC AAC AGG ACC CTC CAC GTC AGC ATG TTC CAG Pro Ser Ile His Leu Leu Asn Arg Thr Leu His Val Ser Met Phe Gln	145
-105 -100 -95	
GTG GTC CAG GAG CAG TCC AAC AGG GAG TCT GAC TTG TTC TTT TTG GAT Val Val Gln Glu Gln Ser Asn Arg Glu Ser Asp Leu Phe Phe Leu Asp	193
-90 -85 -80	
CTT CAG ACG CTC CGA GCT GGA GAC GAG GGC TGG CTG GTG CTG GAT GTC Leu Gln Thr Leu Arg Ala Gly Asp Glu Gly Trp Leu Val Leu Asp Val	241
-75 -70 -65	
ACA GCA GCC AGT GAC TGC TGG TTG CTG AAG CGT CAC AAG GAC CTG GGA Thr Ala Ala Ser Asp Cys Trp Leu Leu Lys Arg His Lys Asp Leu Gly	289
-60 -55 -50	
CTC CGC CTC TAT GTG GAG ACT GAG GAT GGG CAC AGC GTG GAT CCT GGC Leu Arg Leu Tyr Val Glu Thr Glu Asp Gly His Ser Val Asp Pro Gly	337
-45 -40 -35 -30	
CTG GCC GGC CTG CTG GGT CAA CGG GCC CCA CGC TCC CAA CAG CCT TTC Leu Ala Gly Leu Leu Gly Gln Arg Ala Pro Arg Ser Gln Gln Pro Phe	385
-25 -20 -15	
GTG GTC ACT TTC TTC AGG GCC AGT CCG AGT CCC ATC CGC ACC CCT CGG Val Val Thr Phe Phe Arg Ala Ser Pro Ser Pro Ile Arg Thr Pro Arg	433
-10 -5 1	
GCA GTG AGG CCA CTG AGG AGG CAG CCG AAG AAA AGC AAC GAG CTG Ala Val Arg Pro Leu Arg Arg Gln Pro Lys Lys Ser Asn Glu Leu	481
5 10 15	
CCG CAG GCC AAC CGA CTC CCA GGG ATC TTT GAT GAC GTC CAC GGC TCC Pro Gln Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser	529
20 25 30 35	
CAC GGC CGG CAG GTC TGC CGT CGG CAC GAG CTC TAC GTC AGC TTC CAG His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln	577
40 45 50	
GAC CTT GGC TGG CTG GAC TGG GTC ATC GCC CCC CAA GGC TAC TCA GCC Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala	625
55 60 65	
TAT TAC TGT GAG GGG GAG TGC TCC TTC CCG CTG GAC TCC TGC ATG AAC Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn	673
70 75 80	

GCC ACC AAC CAC GCC ATC CTG CAG TCC CTG GTG CAC CTG ATG AAG CCA	721
Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro	
85 90 95	
AAC GCA GTC CCC AAG GCG TGC TGT GCA CCC ACC AAG CTG AGC GCC ACC	769
Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr	
100 105 110 115	
TCT GTG CTC TAC TAT GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC	817
Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His	
120 125 130	
CGC AAC ATG GTG GTC AAG GCC TGC GGC TGC CAC TGAGTCAGCC CGCCCAGCCC	870
Arg Asn Met Val Val Lys Ala Cys Gly Cys His	
135 140	
TACTGCAGCC ACCCTTCTCA TCTGGATCGG GCCCTGCAGA GGCAGAAAAC CCTTAAATGC	930
TGTCACAGCT CAAGCAGGAG TGTCAGGGGC CCTCACTCTC GGTGCCTACT TCCTGTCAGG	990
CTTCTGGGAA TTC	1003

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro Ala
 -139 -135 -130 -125

Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Val Pro Ser
 -120 -115 -110

Ile His Leu Leu Asn Arg Thr Leu His Val Ser Met Phe Gln Val Val
 -105 -100 -95

Gln Glu Gln Ser Asn Arg Glu Ser Asp Leu Phe Phe Leu Asp Leu Gln
 -90 -85 -80

Thr Leu Arg Ala Gly Asp Glu Gly Trp Leu Val Leu Asp Val Thr Ala
 -75 -70 -65 -60

Ala Ser Asp Cys Trp Leu Leu Lys Arg His Lys Asp Leu Gly Leu Arg
 -55 -50 -45

Leu Tyr Val Glu Thr Glu Asp Gly His Ser Val Asp Pro Gly Leu Ala
 -40 -35 -30

Gly Leu Leu Gly Gln Arg Ala Pro Arg Ser Gln Gln Pro Phe Val Val
 -25 -20 -15

Thr Phe Phe Arg Ala Ser Pro Ser Pro Ile Arg Thr Pro Arg Ala Val
 -10 -5 1 5

Arg Pro Leu Arg Arg Gln Pro Lys Lys Ser Asn Glu Leu Pro Gln
 10 15 20

Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser His Gly
 25 30 35

Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu
 40 45 50

Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr
 55 60 65

Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr
 70 75 80 85

Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro Asn Ala
 90 95 100

Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val
 105 110 115

Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn
 120 125 130

Met Val Val Lys Ala Cys Gly Cys His
 135 140

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Glu Leu
1 5 10 15

Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Leu Leu Val Ile Ala Pro
20 25 30

Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu
35 40 45

Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val
50 55 60

His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro Thr
65 70 75 80

Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val
85 90 95

Ile Leu Arg Lys His Arg Asn Met Val Val Arg Ala Cys Gly Cys His
100 105 110

41
SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Hewick, Rodney M.
Wang, Jack H.
Wozney, John M.
Celeste, Anthony J.

(ii) TITLE OF INVENTION: Bone and Cartilage Inductive Proteins

(iii) NUMBER OF SEQUENCES: 12

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Legal Affairs, Genetics Institute, Inc.
(B) STREET: 87 CambridgePark Drive
(C) CITY: Cambridge
(D) STATE: MA
(E) COUNTRY: USA
(F) ZIP: 02140

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: US
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Kapinos, Ellen J.
(B) REGISTRATION NUMBER: 32,245
(C) REFERENCE/DOCKET NUMBER: GI 5182A

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 617-876-1170
(B) TELEFAX: 617-876-5851

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp Trp
 1 5 10 15

Val Ile Ala Pro Gln Gly Tyr
 20

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus
- (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile
 1 5 10 15

Leu Arg

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus
- (F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Ala Cys Cys Ala Pro Thr Lys

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bos taurus
(F) TISSUE TYPE: Bone

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Thr Asn Glu Leu Pro Pro Pro Asn Lys Leu Pro Gly Ile Phe Asp Asp
1 5 10 15

Val His Gly Ser His Gly Arg
20

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 80 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bos taurus

(vii) IMMEDIATE SOURCE:
(B) CLONE: acc30

(viii) POSITION IN GENOME:
(C) UNITS: bp

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 25..57

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GGATCCGCGT GCTGTGCTCC GACC AAG CTG AGC GCC ACC TCC GTG CTC TAC
Lys Leu Ser Ala Thr Ser Val Leu Tyr
1 5

TAC GAC AGCAGCAACA ATGTAATTCT AGA

Tyr Asp

10

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 11 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 199 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Bos Taurus

(vii) IMMEDIATE SOURCE:

(A) LIBRARY: Bovine genomic
(B) CLONE: Lambda 9800-10

(viii) POSITION IN GENOME:

(C) UNITS: bp

(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 30..199

(ix) FEATURE:

(A) NAME/KEY: intron
(B) LOCATION: 1..29

(ix) FEATURE:

(A) NAME/KEY: CDS
(B) LOCATION: 30..179

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TGCCCGCTGC CCCCTCCCGC CCCCCGCCAG GTG CAC CTG CTG AAG CCG CAC GCG
Val His Leu Leu Lys Pro His Ala

1

5

GTC CCC AAG GCG TGC TGC GCG CCC ACC AAG CTG AGC GCC ACT TCC GTG	45	101	
Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val			
10	15	20	
CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC CGC AAC		149	
Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn			
25	30	35	40
ATG GTG GTC CGC GCC TGC GGC TGC CAC	TGAGGCCCA ACTCCACCGG	196	
Met Val Val Arg Ala Cys Gly Cys His			
45	50		
CAG		199	

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 49 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Val His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro				
1	5	10	15	
Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn				
20	25	30		
Val Ile Leu Arg Lys His Arg Asn Met Val Val Arg Ala Cys Gly Cys				
35	40	45		

His

(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 172 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Bos taurus

(vii) IMMEDIATE SOURCE:

- (A) LIBRARY: Bovine genomic
- (B) CLONE: Lambda 9800-10

(viii) POSITION IN GENOME:

(C) UNITS: bp

46

(ix) FEATURE:

- (A) NAME/KEY: exon
- (B) LOCATION: 51..161

(ix) FEATURE:

- (A) NAME/KEY: intron
- (B) LOCATION: 1..50

(ix) FEATURE:

- (A) NAME/KEY: intron
- (B) LOCATION: 162..172

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 51..161

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GGGGTGGGAG GGCACGTGGA TGGGACTCAC CTTCTCCCAC TACCCCCAG GAC TGG 56
Asp Trp
1

GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG GAG TGC 104
Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys
5 10 15

TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG 152
Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu
20 25 30

CAG TCC CTG GTCAGTACCT C 172
Gln Ser Leu
35

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 37 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly 15
1 5 10 15

Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala 30
20 25 30

Ile Leu Gln Ser Leu
35

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 119 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Bos taurus
- (vii) IMMEDIATE SOURCE:
 - (A) LIBRARY: Bovine genomic
 - (B) CLONE: Lambda 9800-10
- (viii) POSITION IN GENOME:
 - (C) UNITS: bp
- (ix) FEATURE:
 - (A) NAME/KEY: exon
 - (B) LOCATION: 20..99
- (ix) FEATURE:
 - (A) NAME/KEY: intron
 - (B) LOCATION: 1..19
- (ix) FEATURE:
 - (A) NAME/KEY: intron
 - (B) LOCATION: 100..119
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 22..99

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

CCCTTGCAGT TCCCCGCAGA C GAC GTC CAC GGC TCC CAC GGC CGG CAG GTG Asp Val His Gly Ser His Gly Arg Gln Val 1 5 10	51
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TGC CGT CGG CAC GAG CTG TAC GTG AGC TTC CAG GAC CTG GGC TGG CTG Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu 15 20 25	99
--	----

GTGAGTTCCG ACTCTCCTTT	119
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(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Glu Leu
1 5 10 15

Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu
20 25

48

Sub X conc. 1
C1

GTG CAC CTG CTG AAG CCG CAC GCG GTC CCC AAG GCG TGC TGC GCG CCC
ACC AAG CTG AGC GCC ACT TCC GTG CTC TAC TAC GAC AGC AGC AAC AAC
GTC ATC CTG CGC AAG CAC CGC AAC ATG GTG GTC CGC GCC TGC GGC TGC
CAC (SEQ ID NO: 7);

5

b)

GAC TGG GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG
GAG TGC TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC
ATC CTG CAG TCC CTG (SEQ ID NO: 9); and

10 c)

GAC GTC CAC GGC TCC CAC GGC CGG CAG GTG
TGC CGTCGG CAC GAG CTG AGC TTC CAG GAC CTG GGC TGG CTG (SEQ ID
NO: 11).

15

d) the nucleotide sequence comprising nucleotide #1 through
(SEQ ID NO: 13)
#843 of Figure 2, and

e) the nucleotide sequence comprising nucleotide #430 through
20 #843 of Figure 2, (SEQ ID NO: 13).

7. An isolated DNA sequence comprising the nucleotide sequence
(SEQ ID NO: 13)
set forth in Figure 2, from nucleotide #1 to #843.

25 8. An isolated DNA sequence comprising the nucleotide sequence
(SEQ ID NO: 13)
set forth in Figure 2, from nucleotide #430 through #843.

9. The DNA sequence of ATCC #75010 encoding BMP-8.

10. A purified protein produced by the steps of:

(a) culturing a cell transformed with a vector comprising
5 a DNA sequence of claim 6 said DNA sequence in operative
association with an expression control sequence therefor;

and

(b) recovering, isolating and purifying from said culture
medium 10 a protein characterized by the ability to induce
cartilage and/or bone formation.

11. A purified protein produced by the steps of:

(a) culturing a cell transformed with a vector containing
15 the DNA sequence of claim 9 encoding BMP-8 said sequence
in operative association with an expression control sequence
therefor; and

(b) recovering, isolating and purifying from said culture
medium a BMP-8 protein characterized by the ability to
induce cartilage and/or bone formation.

20 12. A purified BMP-8 protein produced by the steps of

(a) culturing a cell transformed with a vector having a
DNA sequence of claim 7 said DNA sequence in operative
25 association with an expression control sequence therefore;
and

expression control sequence therefor; and

(b) recovering, isolating and purifying from said culture medium a protein characterized by the ability to induce cartilage and/or bone formation.

19. A method for producing a purified BMP-8 protein said method comprising the steps of:

(a) culturing a cell transformed with a vector having a DNA sequence comprising nucleotide #1 through #843 of Figure 2 said DNA sequence in operative association with an expression control sequence therefore; and

(b) recovering, isolating, and purifying from said culture medium a protein characterized by an amino acid sequence comprising amino acid #143 to #281 of Figure 2^(SEE ID NG:14)

20. A pharmaceutical composition comprising an effective amount of a BMP-8 protein in admixture with a pharmaceutically acceptable vehicle.

21. A pharmaceutical formulation for bone and/or cartilage formation comprising an effective amount of a BMP-8 protein in a pharmaceutically acceptable vehicle.

22. A composition of claim 13 further comprising a matrix for supporting said composition and providing a surface for bone and/or cartilage formation.

23. The composition of claim 14 wherein said matrix comprises a material selected from the group consisting of hydroxyapatite, collagen, polylactic acid and tricalcium phosphate.

5

24. A pharmaceutical composition for wound healing and tissue repair said composition comprising an effective amount of a BMP-8 protein in a pharmaceutically acceptable vehicle.

10 25. A BMP-8 protein comprising a disulfide-linked dimer wherein at least one subunit comprises amino acid #143 through #281 of Figure 2, (SEQ ID NO:14).

a

ABD
34

a